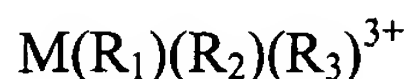


AMENDMENTS

COMPLETE LISTING OF THE CLAIMS:

Upon entry of the amendment, the claims will be pending as follows:

1. (Currently amended) A compound of the formula:

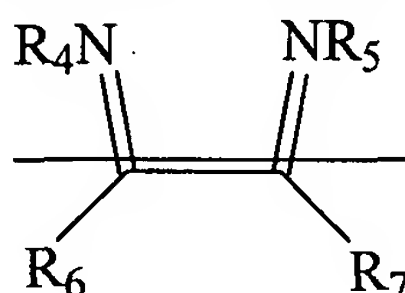


wherein:

M is a suitable photoexcitable metal,

R₁ and R₂ are ligands which are each independently ethylenediamine or a substituted derivative thereof, or substituted or unsubstituted aryl or heteroaryl of 1 to 5 rings, and

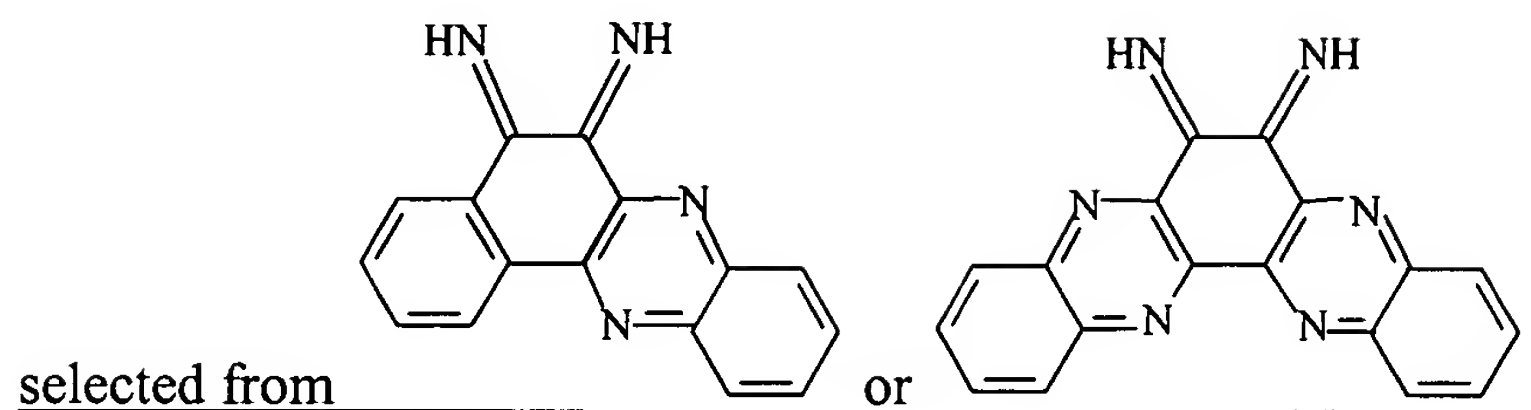
~~R₃ is a ligand having the following structure:~~



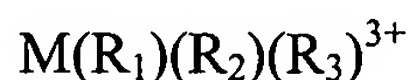
~~wherein:~~

~~R₄ and R₅ are H or lower alkyl,~~

~~R₆ and R₇ are taken together to form a substituted or unsubstituted, fused aromatic or heteroaromatic ring system comprising at least four rings, wherein each ring contains from 0 to about 3 heteroatoms; and wherein substituents on said substituted rings are H, R, halo, OH, OR, NH₂, NHR, NR₂, CN, NO₂, SH, SO₃, OSO₃, C(O)OH, C(O)OR, C(O)NH₂, C(O)NHR, C(O)NR₂, SO₃R, or OSO₃R, wherein each R is independently lower alkyl, cycloalkyl, lower alkenyl, lower alkynyl, or phenyl~~



2. (Original) The compound according to claim 1, wherein M is Rh, Ru, Co, Fe, Cr, Cu, Zn, Cd, or Pb.
3. (Original) The compound according to claim 1, wherein R₁ and R₂ are bidentate ligands.
4. (Original) The compound according to claim 3, wherein R₁ and R₂ are each independently 2,2'-bipyridine, 4,4'-dimethyl-2,2'-bipyridine, or 4,4'-diamido-2,2'-bipyridine.
- 5-9 (Cancelled)
10. (Currently amended) A method for detecting a base-pair mismatch in a nucleic acid duplex, said method comprising forming a complex comprising said nucleic acid duplex and a compound having the following formula:

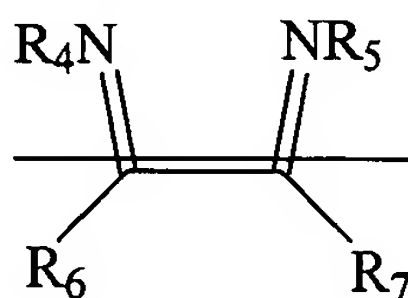


wherein:

M is a suitable photoexcitable metal,

R₁ and R₂ are ligands which are each independently ethylenediamine or a substituted derivative thereof, or substituted or unsubstituted aryl or heteroaryl of 1 to 5 rings, and

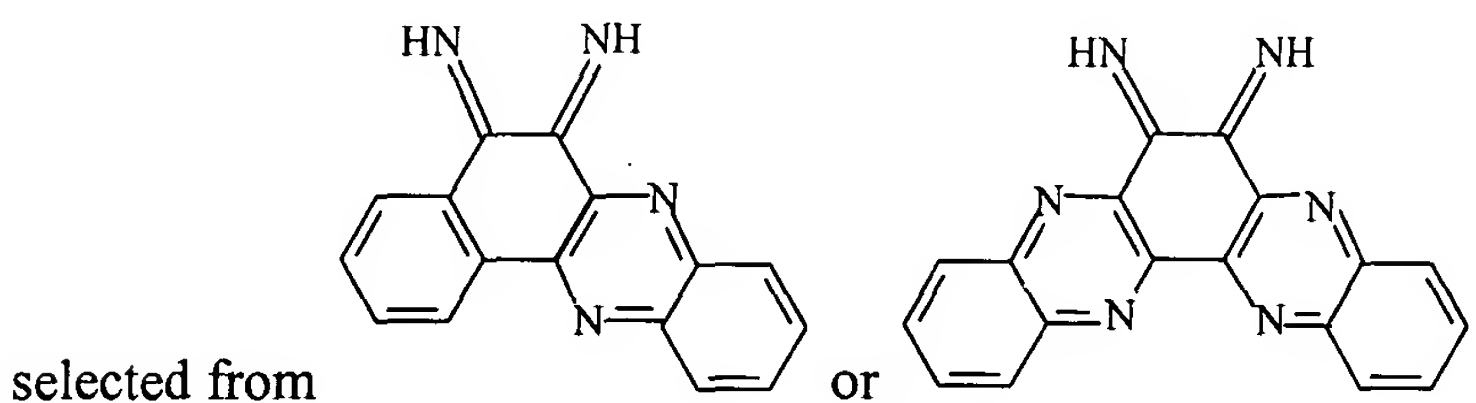
R₃ is a ligand having the following structure:



wherein:

~~R₄ and R₅ are H or lower alkyl,~~

~~R₆ and R₇ are taken together to form a substituted or unsubstituted, fused aromatic or heteroaromatic ring system comprising at least four rings, wherein each ring contains from 0 to about 3 heteroatoms; and wherein substituents on said substituted rings are H, R, halo, OH, OR, NH₂, NHR, NR₂, CN, NO₂, SH, SO₃, OSO₃, C(O)OH, C(O)OR, C(O)NH₂, C(O)NHR, C(O)NR₂, SO₃R, or OSO₃R, wherein each R is independently lower alkyl, cycloalkyl, lower alkenyl, lower alkynyl, or phenyl, and subjecting said complex to conditions allowing detection of a signal, wherein the presence of a signal is indicative of the presence of a base-pair mismatch~~

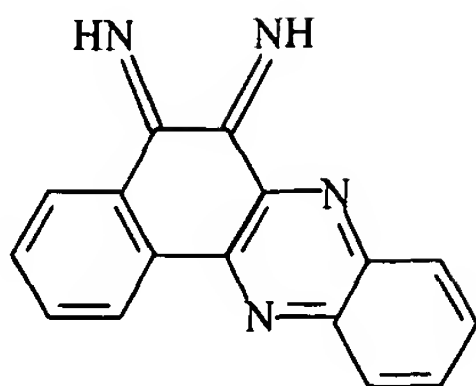


11. (Original) The method of claim 10, further comprising exposing the nucleic acid duplex and the compound to cleavage conditions, and determining the presence or absence of cleavage products, whereby the presence of cleavage products is indicative of a base-pair mismatch.
12. (Original) The method according to claim 10, wherein M is Rh, Ru, Co, Fe, Cr, Cu, Zn, Cd, or Pb.
13. (Original) The method according to claim 10, wherein said compound has the structure wherein:

M is Rh or Ru,

R₁ and R₂ are each 2,2'-bipyridine, and

R₃ is

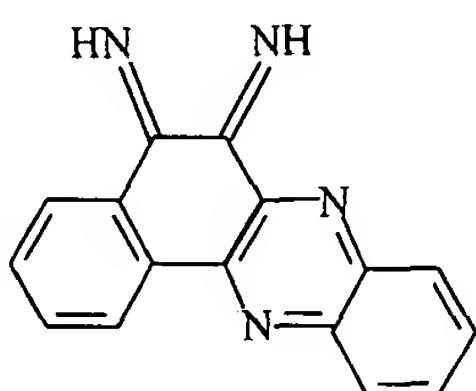


14. (Original) The method according to claim 13, wherein said compound has the structure wherein:

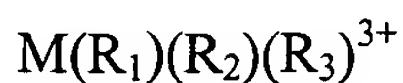
M is Rh,

R₁ and R₂ are each 2,2'-bipyridine, and

R₃ is



15. (Currently amended) A method for detecting a base-pair mismatch in a nucleic acid duplex, said method comprising forming a complex comprising said nucleic acid duplex and a compound having the following formula:

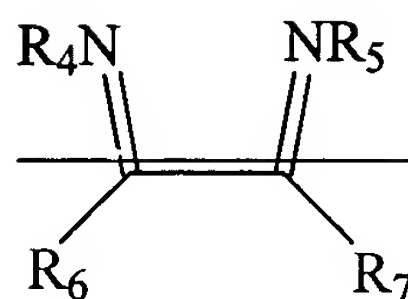


wherein:

M is a suitable photoexcitable metal,

R₁ and R₂ are ligands which are each independently ethylenediamine or a substituted derivative thereof, or substituted or unsubstituted aryl or heteroaryl of 1 to 5 rings,
and

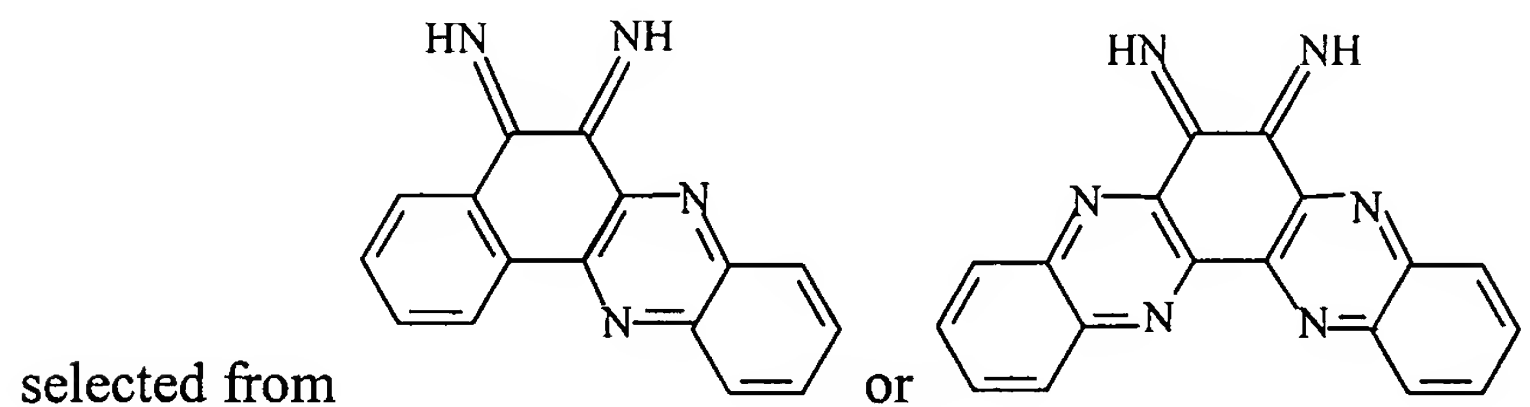
R₃ is a ligand having the following structure:



wherein:

~~R₄ and R₅ are H or lower alkyl,~~

~~R₆ and R₇ are taken together to form a substituted or unsubstituted, fused aromatic or heteroaromatic ring system comprising at least four rings, wherein each ring contains from 0 to about 3 heteroatoms; and wherein substituents on said substituted rings are H, R, halo, OH, OR, NH₂, NHR, NR₂, CN, NO₂, SH, SO₃, OSO₃, C(O)OH, C(O)OR, C(O)NH₂, C(O)NHR, C(O)NR₂, SO₃R, or OSO₃R, wherein each R is independently lower alkyl, cycloalkyl, lower alkenyl, lower alkynyl, or phenyl, and subjecting said complex to cleavage conditions, and determining the presence or absence of cleavage products, whereby the presence of cleavage products is indicative of a base pair mismatch~~



16. (Original) A method for diagnosing a genetic disorder, said method comprising contacting a compound according to claim 1 with a mammalian cell having or suspected of having such a disorder, and optionally treating said cell with sufficient light to cause a detectable signal and/or polynucleotide cleavage, whereby detection of a signal or polynucleotide cleavage fragments is indicative of a genetic disorder.

17. (Original) A method for treating a subject having a genetic disorder characterized by base-pair mismatches in a nucleic acid duplex, said method comprising administering to a subject in need thereof an effective amount of a compound according to claim 1.

18. (Original) The method of claim 17, wherein the compound includes a cytotoxic molecule attached thereto.
19. (Original) A method for detecting base-pair mismatches in nucleic acid duplexes, said method comprising forming a complex comprising said nucleic acid duplex with a compound according to claim 1, subjecting said complex to photocleavage conditions, and determining the presence or absence of cleavage products, whereby the presence of said cleavage products is indicative of a base-pair mismatch.
20. (Original) The method of any of claims 10, 15, 16 or 19, wherein the base-pair mismatch is a single nucleotide polymorphism (SNP).
21. (Original) The method of any of claims 10, 15, 16 or 19, wherein the base-pair mismatch is a guanine-adenine pairing.
22. (Original) The method of any of claims 10, 15, 16 or 19, wherein the base-pair mismatch is an adenine-adenine pairing.
23. (Original) The method of any of claims 10, 15, 16 or 19, wherein the base-pair mismatch is a guanine-guanine pairing, a thymine-thymine pairing, a cytosine-cytosine pairing, a guanine-thymine pairing, a cytosine-thymine pairing, or a cytosine-adenine pairing.
24. (Original) A kit for detecting base-pair mismatches in nucleic acid duplexes, the kit comprising:
carrier means containing therein one or more containers wherein a first container contains a compound according to claim 1.
25. (Original) The kit of claim 24, wherein one other container contains oligonucleotides or a substrate containing oligonucleotides specific for a gene, gene locus, or polynucleotide sequence of interest.
26. (Original) A composition comprising two complementary oligonucleotide strands having a base-pair mismatch, and a compound of the formula $M(R_1)(R_2)(R_3)^{3+}$.

27. (Currently amended) A plurality of sterically demanding intercalating compounds of the formula:

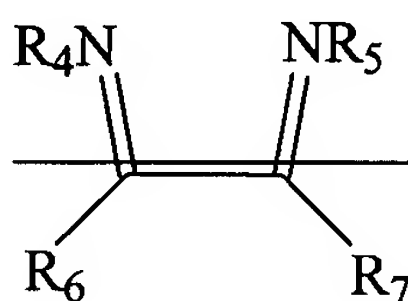


wherein:

M is a suitable photoexcitable metal,

R₁ and R₂ are ligands which are each independently ethylenediamine or a substituted derivative thereof, or substituted or unsubstituted aryl or heteroaryl of 1 to 5 rings, and

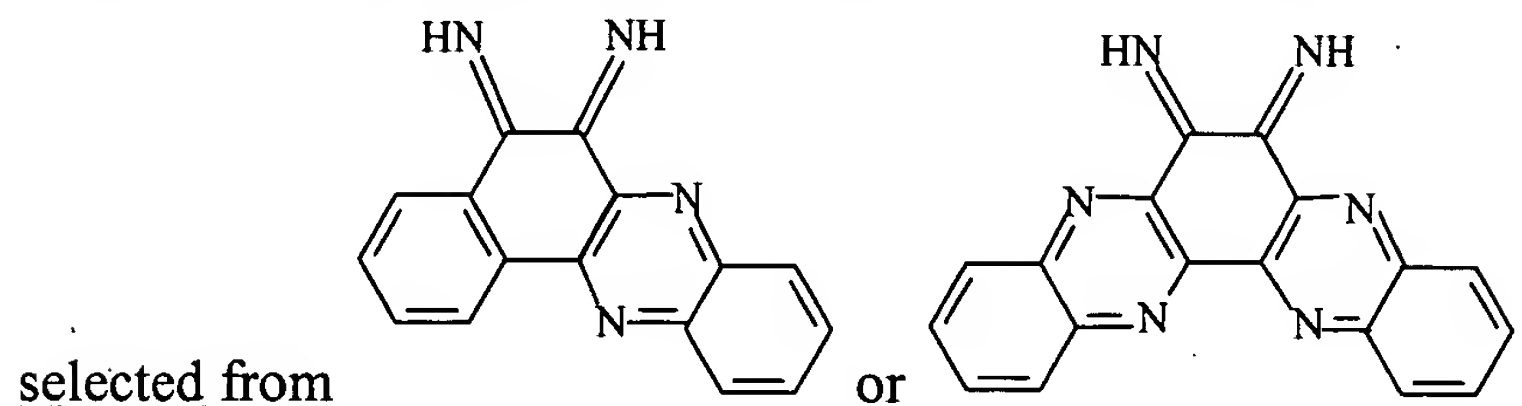
R₃ is a ligand having the following structure:



wherein:

R₄ and R₅ are H or lower alkyl,

R₆ and R₇ are taken together to form a substituted or unsubstituted, fused aromatic or heteroaromatic ring system comprising at least four rings, wherein each ring contains from 0 to about 3 heteroatoms; and wherein substituents on said substituted rings are H, R, halo, OH, OR, NH₂, NHR, NR₂, CN, NO₂, SH, SO₃, OSO₃, C(O)OH, C(O)OR, C(O)NH₂, C(O)NHR, C(O)NR₂, SO₃R, or OSO₃R, wherein each R is independently lower alkyl, cycloalkyl, lower alkenyl, lower alkynyl, or phenyl



REMARKS

A. Regarding the Amendments

Claims 1, 10, 15 and 27 have been amended as set forth in the above complete listing of the claims. As amended, the claims are supported by the specification and the original claims. For example, support for the amendments to these claims may be found in the specification in paragraphs [0033] and [0034]. By the present amendment, cancellation of claims 5-9 is requested, without prejudice. Thus, upon entry of the amendments, claims 1-4 and 10-27 will be pending.

B. Rejection Under 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 1-23 and 26-27 under 35 U.S.C. 102(e) as allegedly anticipated by U.S. Patent No. 6,031,098 (hereinafter "the '098 patent").

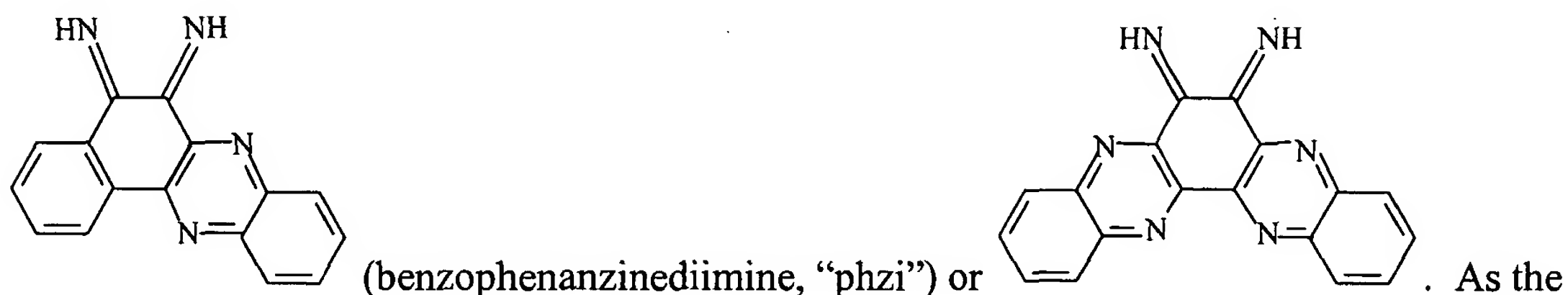
35 U.S.C. 102(e) states that a person shall be entitled to a patent, unless

"the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent."

Applicant respectfully submits that the claimed invention is not anticipated, as the invention has not been fully described in the references cited by the Patent Office.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration (In re Spada, 15 USPQ 2d 1655 (Fed. Cir. 1990), In re Bond, 15 USPQ 2d 1566 (Fed. Cir., 1990). Specifically, it is alleged in the Office Action mailed March 27, 2003 that the '098 patent teaches a compound of the formula recited in Claim 1 of the claimed invention. Applicants respectfully traverse the rejection.

It is alleged in the Office Action mailed March 27, 2003 that the '098 patent teaches a compound of the formula recited in claim 1, as well as the use of the compound. Applicants respectfully disagree. The Examiner's attention is respectfully drawn to the amended claims set forth above in the complete "listing of the claims." The compound of claim 1 is directed to a compound with the formula $M(R_1)(R_2)(R_3)^{3+}$. However, the Examiner's attention is respectfully drawn to the definition of the variable R_3 , where the compounds differ notably. Where the '098 patent describes R_3 as 5,6-chrysene quinone diimine, or "chrysi", the claimed invention claims a compound where R_3 is



cited reference and the claimed invention are not directed to the same compound, it is respectfully submitted that the '098 reference does not teach all of the aspects of the claimed invention and therefore, the '098 reference does not anticipate the claimed reference. Additionally, because the compounds claimed in the '098 patent differ from the compounds recited by claim 1 of the claimed invention, it is respectfully submitted that the methods of use also differ, as they are directed to use of the different compounds.

Similarly, Applicants respectfully traverse the rejection of claims 1-9 and 26-27 under 35 U.S.C. 102(b) as allegedly anticipated by Dandliker. It is alleged in the Office Action mailed March 27, 2003 that Dandliker teaches a compound of the formula recited in claim 1 of the claimed invention. Applicants respectfully disagree. Dandliker does not teach a

metallointercalator where the variable R_3 is phzi or

The image shows the chemical structure of 5,6-chrysene quinone diimine (chrysi), which consists of a central six-membered ring with two imine groups (=NH) at the top, and two benzene rings fused to the sides. The text "Accordingly," is placed after the structure.

Dandliker does not teach a compound of the claimed invention.

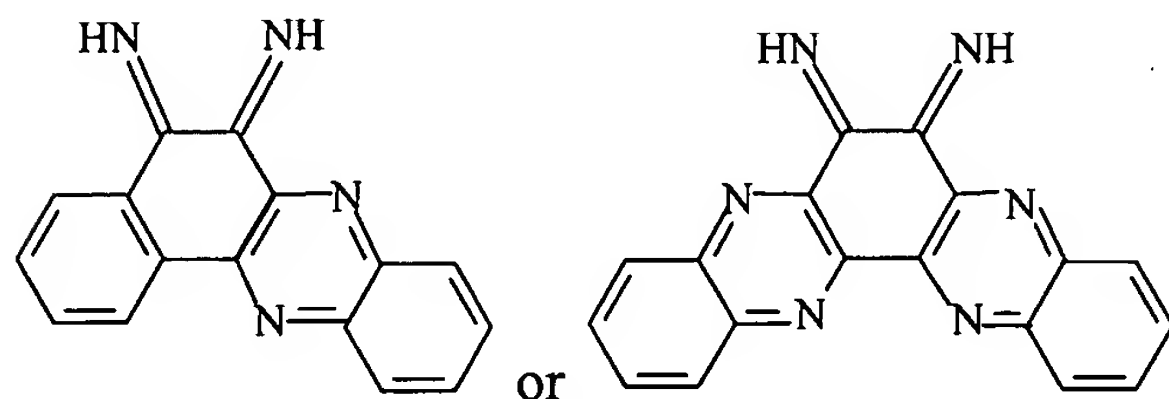
As neither of the cited references, the '098 patent or Dandliker, teaches all of the elements of the cited invention, it is respectfully submitted that the claimed invention is not anticipated under 35 U.S.C. 102(e). Withdrawal of the rejection is therefore respectfully requested.

C. Rejection Under 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 24-25 under 35 U.S.C. 103(a) as allegedly unpatentable over the '098 patent in view of the Stratagene catalog.

In order for an invention to be obvious, the differences between the subject matter of the application and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard, the combination of references must teach or suggest all of the elements of the claimed invention. It is respectfully submitted that the '098 patent in view of the Stratagene catalog does not teach or suggest all of the elements of the claimed invention.

As set forth above, the '098 patent does not teach, nor does it suggest, a compound that is a metalointercalator with a general formula of $M(R_1)(R_2)(R_3)^3$, where the variable R_3 is



The Stratagene reference is cited as teaching the advantages of assembling and utilizing a kit. Therefore it is alleged that together, the '098 patent and Stratagene catalog teach or suggest a kit containing the compound of the '098 reference. However, as the '098 reference does not teach or suggest the compound of the claimed invention, the '098 patent in view of the Stratagene catalog does not teach or suggest a kit containing the compound of the claimed invention. It is therefore respectfully submitted that

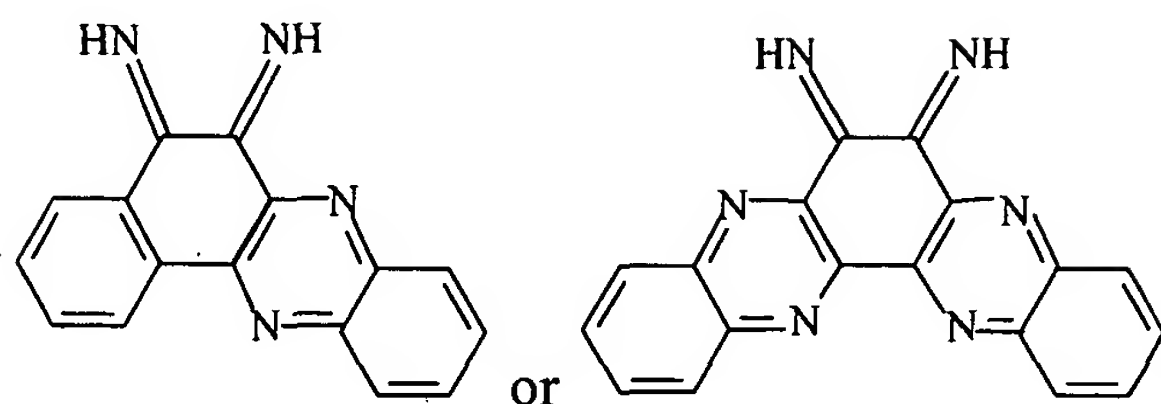
the claimed invention is not obvious, in light of the cited references. Withdrawal of the rejection is therefore respectfully requested.

Additionally, Applicants respectfully traverse the rejection of claims 24-25 under 35 U.S.C. 103(a) as allegedly unpatentable over Dandliker in view of the Stratagene catalog. Utilizing the same reasoning as set forth above with respect to the '098 patent in view of the Stratagene catalog, it is respectfully submitted that while Dandliker in view of the Stratagene catalog may teach or suggest a kit containing the compound of Dandliker, because Dandliker does not teach or suggest the compound of the claimed invention, Dandliker in view of the Stratagene catalog does not teach or suggest a kit containing the compound of the claimed invention. It is therefore respectfully submitted that the claimed invention is not obvious, in light of the cited references. Withdrawal of the rejection is therefore respectfully requested.

As neither the '098 patent in view of the Stratagene catalog, nor Dandliker in view of the Stratagene catalog teaches or suggests a kit containing the compound of the claimed invention, it is respectfully submitted that the claims of the invention are not obvious in view of the cited references. Withdrawal of the rejections of claim 24-25 under 35 U.S.C. 103(a) as allegedly unpatentable is therefore respectfully requested.

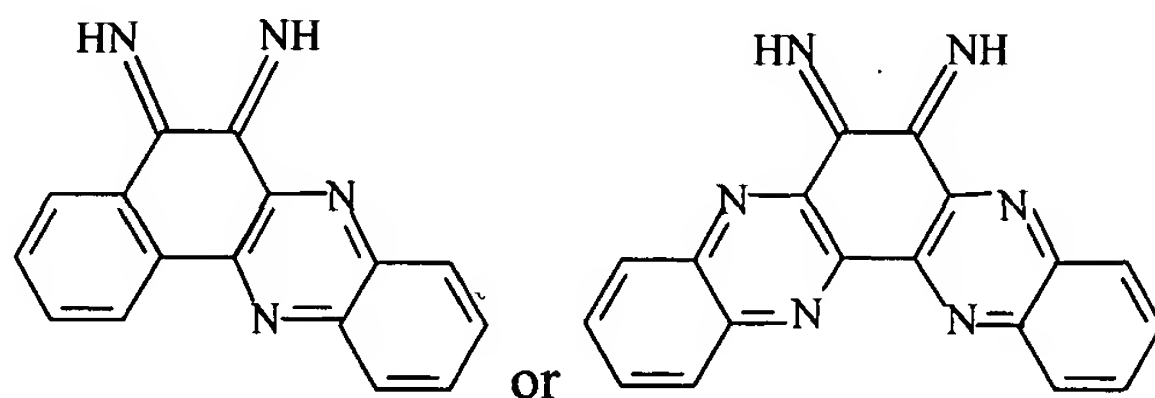
D. Double Patenting Rejection

Applicants acknowledge the rejection of claims 1-9 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting, in light of claims 1-11 of the '098 patent. Applicants respectfully disagree. It is respectfully submitted that when the amended claims of the claimed invention are viewed in light of claims 1-9 of the '098 patent, it is clear that the claims are patentably distinct. The compound of the '098 patent is not disclosed by the claims of the claimed invention, as the compound of the '098 patent does not have



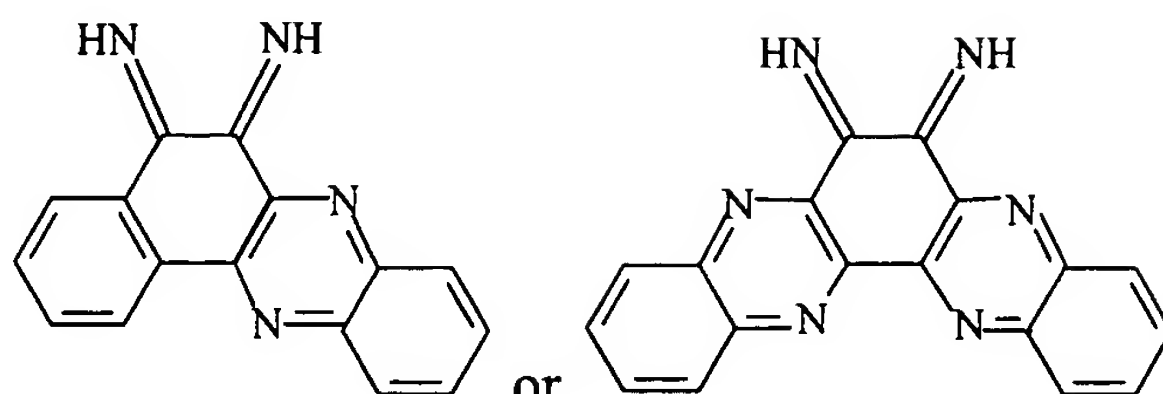
in the R₃ position. As the claims of the claimed invention are patentably distinct from claims 1-9 of the '098 patent, it is respectfully submitted that the two do not provide double patenting of the same invention. Withdrawal of the double patenting rejection is therefore respectfully requested.

Applicants acknowledge the rejection of claims 10-16 and 19-23 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting, in light of claims 1-10 of U.S. Patent No. 6,306,601 (hereinafter "the '601 patent"). The rejection is respectfully traversed, as Applicants submit that the claims of the claimed invention are patentably distinct from claims 1-10 of the '601 patent, as the claims of the '601 patent do not teach or suggest a method utilizing a compound with



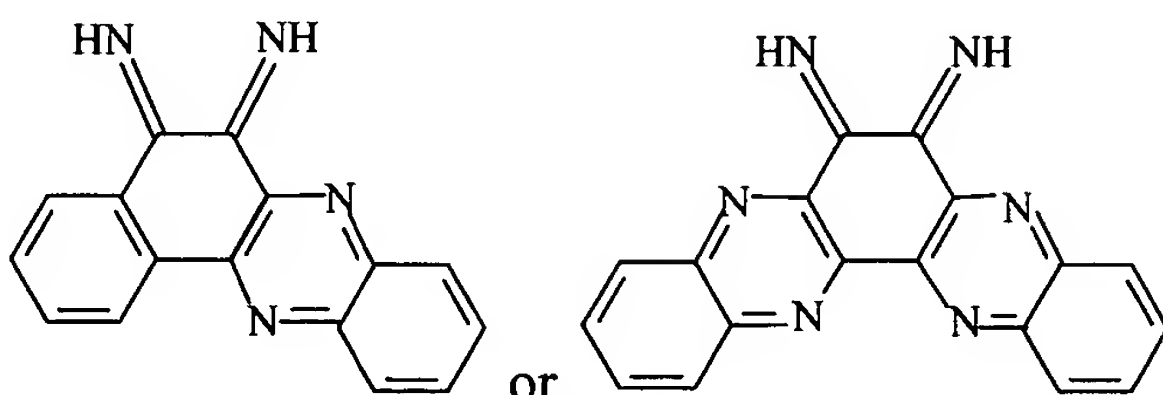
in the R₃ position. Accordingly, withdrawal of the double patenting rejection is respectfully requested.

Applicants acknowledge the rejection of claim 17 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting, in light of claims 1-7 of U.S. Patent No. 6,444,661 (hereinafter "the '661 patent"). The rejection is respectfully traversed, similar to the above traversal, in that Applicants submit that the claims of the claimed invention are patentably distinct from claims 1-7 of the '661 patent, as the claims of the '661 patent do not teach or suggest a method utilizing a compound with



in the R₃ position. Accordingly, withdrawal of the double patenting rejection is respectfully requested.

Applicants acknowledge the rejection of claims 24-26 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting, in light of claims 1-10 of the '601 patent. The rejection is respectfully traversed, similar to the above traversal, in that Applicants submit that the claims of the claimed invention are patentably distinct from claims 1-10 of the '601 patent, as the claims of the '601 patent do not teach or suggest a method utilizing a compound with



in the R₃ position, either in the method of the invention or in a kit of the invention. Accordingly, withdrawal of the double patenting rejection is respectfully requested.

In re Application of:
Barton and Junicke
Application No.: 10/015,997
Filed: December 10, 2001
Page 15

PATENT
Attorney Docket No.: CIT1290-1

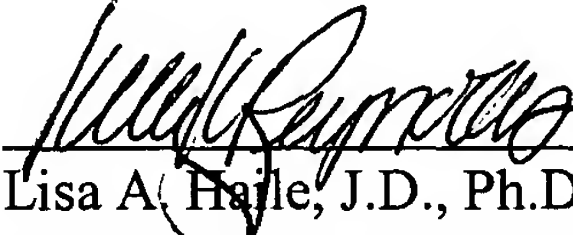
CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 1-4 and 10-27 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: July 28, 2003

 *Reg No. 51,154 for*

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